UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,866	05/16/2006	Bror Morein	72294-82303	6747

21186 7590 06/25/2008

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,866	MOREIN ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 2-4-08.

Claim 1 have been amended. Claims 1-14 are pending.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Rejection to claims 1, 3-4, 9-10, and 14 under 35 USC 102(b) is withdrawn in light of applicant's amendment and in light of applicant's argument.

b) Rejection to claims 1, 3, and 11-13 under 35 USC 103(a) is withdrawn in light of applicant's amendment and in light of applicant's argument.

3. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 is drawn to a method, wherein the saponin fraction from Quil A is fraction of C of Quil A or fractio nB of Quil A. Claim 1 recites a fraction of Quil A, Claim 3 recites that Quil A fraction is either fraction B or c, since claim 1 is already limited to a fraction A. Appropriate correction is advised.

Claim Rejections Maintained- 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. The rejection of claims 1-2, 4-9, and 14 under 35 U.S.C. 102(b) as being anticipated by Friede et al US Patent No. 6,558,670 Date May 6, 2003 is maintained for the reasons set forth in the previous office action.

Applicant arguments:

Claim 1, as amended, recites "[a] method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect comprising an iscom particle comprising fraction A of Quil A together with at least one other adjuvant, wherein the at least one other adjuvant is in free form or integrated into another separate iscom particle other than the one in which the fraction A of Quil A was integrated." Thus, claim 1 is directed an iscom particle comprising fraction A of Quil A and a free form (i.e. not integrated into any iscom particle) of another adjuvant and to an iscom particle comprising fraction A of Quil A and an adjuvant integrated into another separate iscom particle. Therefore, the claim is not directed to an iscom particle comprising both fraction A of Quil A and at least another adjuvant. The iscom particle may be an iscom or an iscom matrix.

U.S. Pat. No. 6,558, 670 (Friede et al.) is directed to vaccines. The abstract discloses adjuvant compositions comprising a saponin and an immunostimulating ologonucleotide. The saponin may be QS 7 of Quil A (column 4 lines 13-14). It is further disclosed that the saponins may be in the form ofiscoms (column 2 lines 11-18). The only example in the patent describes a mixture of Q21 of Quil A, which is close to fraction C of Quil A, and the ologinucleotide CpG. However, the Q21 fraction is not integrated into iscoms in the example.

Applicant respectfully submits that Friede et al. do not disclose that fraction A, QS 7 or Q21 must be in an iscom particle and that any other adjuvant may be in an iscom particle that must be different from the one in which fraction A is integrated. Furthermore, U.S. Pat. No. 6,558, 670 discloses that haemolytic saponins are preferred (column 2 lines 59-62). According to the presently claimed invention, the less

haemolytic saponin of Quil A is chosen, namely fraction A. This less haemolytic fraction of Quil A is furthermore always integrated into an iscom or an iscom matrix particle.

Examiner's Response to Applicant's Arguements:

Examiner accepts Applicants' amendment, however the arguement is not persuasive. Although claim 1 is directed to an iscom particle comprising fraction A of Quil A and a free form (i.e. not integrated into any iscom particle) of another adjuvant and to an iscom particle comprising fraction A of Quil A and an adjuvant integrated into another separate iscom particle. Friede et al teach the CpG used in the adjuvant combinations of the present invention may be in free solution of may be complexed to particulate carriers, for example aluminium or calcium salts, liposomes, ISCOMs, oil in water emulsions, polylactide polyglycolide microparticles, or alginates. Preferably said carriers are cationic. The vaccines of the present invention further comprise an antigen which may be associated with the CpG-carrier complex, or may not be associated with the CpG-carrier complex. In this case, the antigen may be free suspension or associated with a separate carrier (see columns 3-6). Furthermore Friede et al teach that the CpG and saponin in the adjuvants or vaccines of the present invention may be separate or associated. For example, the CpG and saponin may be in free suspension or may be associated via a carrier such as aluminium hydroxide or by a cationic liposome or ISCOM. Also the instant claims are drawn to a method as set forth in the previous office action comprising a fraction of Quil A. Friede et al teach that particularly preferred fractions of Quil A are QS21, QS7, and QS17 (see columns 3-6). There is also no discussion of haemolytic saponins reducing or even eliminating the haemolytic effect. Therefore the limitations have been met.

As outlined previously, the instant claims are drawn to a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect, comprising: an iscom particle comprising a fraction A of Quil A together with at least one other adjuvant is in free form or integrated into another separate iscom particle other than the one in which the fraction A of Quil A was integrated.

Friede et al teach a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect, comprising: an iscom particle comprising a fraction A of Quil A; and together with at least one other adjuvant (CpG) (see example 1). Fried et al teach that the CpG used in the adjuvant combinations of the present invention may be in free solution or may be complexed to ISCOMs. Friede et al teach that the CpG and saponin in the adjuvants or vaccines of the present invention may be separate or associated. Therefore the method of Fried et method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect, comprising: an iscom particle comprising a fraction A of Quil A; and together with at least one other adjuvant, in free form or integrated into another separate iscom particle, wherein said at least one other adjuvant is integrated into one iscom particle, wherein said fraction A of Quil A is integrated into a first iscom particle and said at least one other adjuvant is integrated into a second iscom particle, wherein said at least one other adjuvant is integrated into a plurality of separate iscom particles (see "Detailed Description"). Friede et al teach that the haemolytic saponin preparations will further be combined with other adjuvants including Monophosphoryl Lipid A therefore the method of Fried et al teach the method according to claim 1 wherein said one other adjuvant is monophosphoryl lipid A and the method according to claim 7 wherein said at least one other adjuvant is at least one of Monophosphoryl Lipid A (see "Detailed Description"). Friede et al teach the method wherein said iscom particle is an iscom complex (Quil A, cholesterol, adjuvant), wherein in the composition further comprises a pharmaceutically acceptable carrier (see abstract).

New Grounds of Rejections

Claim Rejections Maintained- 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3, 10-13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Friede et al US Patent No. 6,558,670 Date May 6, 2003 in view of Cox et al WO 96/11711 Date April 25, 1996.

Claims 1, 3, 10-13 are drawn to a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect, comprising: an iscom particle comprising a fraction A of Quil A together with at least one other adjuvant is in free form or integrated into another separate iscom particle other than the one in which the fraction A of Quil A was integrated.

Friede et al is relied upon as set forth supra. However Friede et al does not teach a method, wherein the saponin fraction from Quil A is fraction C of Quil A or fraction B of Quil A, wherein iscom particle is iscom matrix complex, wherein the composition comprises 50-99.9% of fragment A of Quil A; and 0.1-50% of a fraction or derivative of

Quil A based on the total weight of the composition, wherein the composition comprises 75-99.9% of fragment A of Quil A; and 0.1-25% of a fraction or derivative of Quil A based on the total weight of the composition, wherein the composition comprises 91-99.1% of fragment A of Quil A; and 0.1-9% of a fraction or derivative of Quil A based on the total weight of the composition.

Cox et al teaches a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect (see pgs. 9-24). The method of Cox et al teach that an iscom matrix can have at least one immunogen (adjuvant), incorporated into or associated with the iscom matrix. Therefore the method of Cox et al teach a method of enhancement of an immune response and immunomodulating activity comprising administration to a subject an effective amount of an adjuvant composition with synergistic effect, comprising: an iscom particle comprising a fraction A of Quil A; and together with at least one other adjuvant, in free form or integrated into another separate iscom particle, wherein at least one other adjuvant is integrated into one iscom particle (see pg. 3 lines 20-30, pgs. 4-5). Cox et al teach the method wherein the saponin fraction from Quil A is fraction B of Quil A, wherein said iscom particle is an iscom complex, wherein said iscom particle is an iscom matrix complex (see page 7 line 24).

As to the limitation of 11-13 is drawn to a method according to claim 3, wherein the composition comprises 50-99.9% of fragment A of Quil A; and 0.1-50% of a fraction or derivative of Quil A based on the total weight of the composition (claim 11), wherein the composition comprises 75-99.9% of fragment A of Quil A; and 0.1-25% of a fraction or derivative of Quil A based on the total weight of the composition(claim 12), wherein the composition comprises 91-99.1% of fragment A of Quil A; and 0.1-9% of a fraction or derivative of Quil A based on the total weight of the composition (claim 13). Cox et al. teaches saponin preparation of saponins of Quillaja saponaria from 50 to 90% by weight of Fraction A and from 50 to 10% by weight of Fraction C, 50 to 70% by weight of fraction A and from 50 to 30% by weight of fraction C, about 70% by weight of fraction

A, about 30% by weight of fraction C, fractions A, B, and C (page 7, line 24). However, it does not teach the specific percentage weight claimed.

The references also do not specifically teach adding the ingredients in the amounts claimed by applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233, 235 (CCPA 1955). Thus, optimization of general conditions is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

Status of the Claims

5. No claims are allowed.

Claims 1-14 are rejected.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nina A Archie/
Examiner, Art Unit 1645
/N. A. A./
Examiner, Art Unit 1645

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Mark Navarro/

Primary Examiner, Art Unit 1645